

Early career forum

ERS International Congress 2019: highlights from Best Abstract awardees

During the 2019 European Respiratory Society (ERS) International Congress in Madrid (Spain), the author of the Best Abstract (highest average score of abstract reviewers and only those who had not applied for a sponsored award) of every Assembly was awarded with a prize. Best Abstract awardees were invited to write a short summary of their congress experience and view on the evolving field of research in light of their respective assembly. The purpose of this article is to give the readers an overview of some of the congress highlights and to give a stage to the promising best-abstract awardees, as they are the future of the ERS.

Assembly 1: general pneumology (Lorna E. Latimer)

The functional capacity and physical activity status of people with respiratory diseases plus the effects of pulmonary rehabilitation dominated the congress agenda. Physical function assessed by 4-m gait speed showed prognostic value in COPD [1]. In asthma, both increasing habitual physical activity [2] and a 3-week intensive pulmonary rehabilitation programme [3] increased asthma control.

Evidence that pulmonary rehabilitation improves more than just exercise capacity was demonstrated across several sessions. Pulmonary rehabilitation performed favourably compared to an inhaled long-acting muscarinic antagonist in COPD for measures of symptom burden, health-related quality of

life (HRQoL) and dyspnoea [4] while cognitive function improved in COPD after pulmonary rehabilitation [5]. Striking data on >7000 clinical patients in England and Wales (UK) demonstrated a survival advantage in patients who completed pulmonary rehabilitation that was independent of disease severity [6].

On the delivery of pulmonary rehabilitation, the Clinical Year in Review session highlighted that patients with COPD and exercise-induced desaturation benefitted from pulmonary rehabilitation without the need for supplemental oxygen [7] while home-based pulmonary rehabilitation may be useful for patients who cannot or do not engage in conventional outpatient pulmonary rehabilitation [8]. Pulmonary telerehabilitation produced similar results to conventional pulmonary rehabilitation but in both groups, short-term improvements were not maintained at 12 months [9]. A post-pulmonary rehabilitation maintenance programme showed encouraging results (although not a randomised trial) with the intervention group maintaining exercise capacity and HRQoL for 4 years and breathlessness scores for 5 years post-rehabilitation [10]. However, maintaining physical activity levels in COPD patients may be difficult if they live in a rainy climate [11].

In COPD experimental exercise physiology, transcutaneous electrical nerve stimulation did not improve exercise capacity (by disrupting muscle afferent feedback) but offered further avenues to explore in this fascinating area [12],

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while eccentric cycling exercise generated lower lactic acid accumulation and less dyspnoea than concentric cycling [13].

Assembly 2: respiratory intensive care (Marieke Duiverman)

It is an interesting time for respiratory intensive care and home noninvasive ventilation (NIV). A new evolving therapy is nasal high-flow therapy (nHFT), and studies have been presented on its use in the intensive care unit [14], in stable COPD during exercise [15] and in interstitial lung disease (ILD) [16]. In the coming years, more data will be available showing the (added) value of nHFT in chronic care, hopefully showing which patient groups benefit. Chronic NIV studies mainly focussed on optimisation of ventilation techniques, initiation and follow-up strategies. Randomised controlled trials (RCTs) were presented showing that (telemonitored) home initiation of NIV is noninferior to in-hospital initiation (in COPD [17], in neuromuscular disease [18] and in obesity hypoventilation syndromes [19]), although the additional benefit in terms of costs seems to depend on the diagnosis, and strategy of NIV initiation and follow-up. Furthermore, in the poster discussion session “Hot topics in non-invasive ventilation”, it became evident that real-life strategies of initial evaluation, selection of patients and follow-up are often different from those used in RCTs, indicating that there might be too little insight into barriers and facilitators of implementing evidence-based care. There were presentations about measuring patient-ventilator asynchrony (PVA), based on flow and airway pressure, in a sophisticated automatic way [20]. This strategy is attractive as it requires only minimal additional measurements and data can be post-processed to derive an asynchrony index. However, further studies must prove whether this strategy identifies all relevant PVAs adequately and whether these PVAs are associated with important patient outcomes [21]. Overall, to improve care, monitoring chronic ventilatory assistance should be practical and lead to worthwhile benefits. We are currently at the border of a new area of displacing ventilatory assistance more and more to the home while improving NIV quality by more sophisticated, easy-to-handle, technically optimised and worthwhile (tele)monitoring.

Assembly 5: airway diseases, asthma and COPD (Mahmoud I. Abdel-Aziz)

In 2019, the ERS Congress included several sessions in asthma, COPD and airway diseases ranging from basic to translational and clinical aspects. Speakers

in the “It takes two to tango: translating scientific findings into clinical applications” symposium showed how basic science can be translated into clinical application in two major airway diseases: asthma and COPD. For example, Marco Contoli discussed how functional imaging techniques can quantify the contribution of small airways as compared to emphysema, and how this could predict lung function decline and disease prognosis in COPD patients [22, 23]. A hot topic oral session was “Beyond type 2 mechanisms in asthma: who are the other players?”, during which speakers discussed potential biomarkers such as neutrophils, microbiota and sex hormones that could direct diagnostic/therapeutic decisions in non-type 2 asthma.

Numerous original studies were also presented. For example, during “The microbiome: novel data across respiratory diseases” session, Aocáin *et al.* [24] characterised the airway resistome in chronic respiratory diseases using a metagenomics approach. They showed that COPD and bronchiectasis patients had a higher abundance of multiple antibiotic resistance genes as compared to severe asthmatics and healthy controls. A study by WEDZICHA *et al.* [25] during the “Exacerbations and clinical impact of airway diseases” session, showed that treatment with tiotropium/olodaterol reduced exacerbation rates compared with tiotropium in a *post hoc* analysis of 9942 COPD patients. Moreover, during the “Precision meets immunology in treatment of airway diseases” session, benralizumab was reported by SCHWEFEL *et al.* [26] to reduce the high-affinity immunoglobulin E receptor on plasmacytoid dendritic cells in 20 severe asthmatics.

In summary, the 2019 Congress covered a broad range of comprehensive topics that provide more understanding into the underlying pathophysiological mechanisms and treatment approaches of airway diseases, asthma and COPD.

Assembly 6: epidemiology and environment (Gulser Caliskan)

Assembly 6 provides an interdisciplinary approach to cover various topics spanning from cutting-edge molecular epidemiology of lung function to clinical, occupational and environmental epidemiology of respiratory disease, in addition, giving emergent insights on consumption of tobacco products and their control [27].

KHAN *et al.* [28] showed that asthmatic mothers who smoked during pregnancy were at greater risk of adverse pregnancy outcomes such as premature birth, low birth weight and small for gestational age. FELIU and coworkers [29, 30] showed that tobacco control could result in a lower prevalence of smokers and higher quit ratios. Therefore, comprehensive tobacco control policies should be considered as they are key to reducing the prevalence of smoking and to

enhancing tobacco cessation rates in their population. They also highlighted that social inequalities in heavy smoking necessitates interventions tailored to vulnerable groups. RAVARA *et al.* [31] reported that prevalence and trends of tobacco use among inpatients are similar to those observed in the general population. Therefore, a variety of screening strategies of tobacco use among inpatients will be crucial in the future and a systematic, system-level approach in hospitals to quit smoking is recommended. During the “From the health effects of tobacco to the epidemiology of tobacco/electronic nicotine delivery system use” session CALISKAN *et al.* [32] showed that the rates of smoking initiation during young adolescence (11–15 years) increased steeply between 1925 and 1980 in females in Australia. After being relatively stable, the rates of smoking initiation increased after the 1970s in males. In the same period, rates in males (16–20 years) decreased steeply, whereas they increased in females. Initiation rates among young adults (21–35 years) decreased steadily for males, while they started to decrease after the 1950s in females [32]. Increased rates of tobacco consumption among young women is worrying not only for health effects in later life but also because tobacco consumption during a susceptible time window may impact subsequent generations, possibly through epigenetic mechanisms [33]. Tobacco control activities during the 90’s are likely to have contributed to the decline in smoking prevalence during recent decades but their effect on smoking initiation should be further investigated. Moreover, a particular focus should be given to the effect of tobacco control activities during pregnancy.

Assembly 7: paediatrics (Sara M. Mensink-Bout)

Life-course studies that showed that lower lung function and asthma in early childhood track into adulthood and might predict the onset of COPD later in life are a hot topic in the field of paediatric respiratory diseases [34, 35]. It was emphasised that insight into the modifiable risk factors of lower lung function and asthma development might provide a window of opportunity for preventive strategies. Recent research presented at the Congress therefore focused on potential risk factors including exposure to environmental factors such as air pollution [36] and phenolic compounds [37], lifestyle factors such as maternal smoking [38] and a selective iron supplementation regime during pregnancy [39], and growth factors including a “low birth size–slower body mass index gain” trajectory [40] and visceral adiposity [41] and their relation with respiratory morbidity. In addition, sophisticated epidemiological approaches to study the combined effect of early life exposures and their relation to respiratory morbidity were discussed. For example, one study used an exposome approach and observed a potential

adverse effect of several chemicals on lung function in children [42]. From a more clinical perspective, highlights of past years were the translation of the current scientific knowledge into clinical guidelines on which symposia were held at the ERS Congress. In the symposium on asthma management, it was emphasised that children with asthma should not be treated with a short-acting β -agonist alone [43]. Evidence on the long-term management of children with bronchopulmonary dysplasia is scarce; in the symposium, it was suggested that these children should not be treated with inhaled or systemic corticosteroids and that a multidisciplinary approach for the long-term management of bronchopulmonary dysplasia is needed [44]. For chronic cough in children, it was highlighted that persistent bacterial bronchitis is a common, but often unrecognised, cause of wet cough in children that can be treated with antibiotics [45]. Furthermore, complex clinical cases were discussed with the audience and a panel of experts, including the case of a 4-month old girl with pleural effusions who appeared to have a chylothorax [46]. Overall, the 2019 ERS International Congress provided a broad overview of paediatric respiratory diseases, ranging from state-of-the-art research to the early origins of lung diseases, and to the presentation and discussion of evidence-based clinical guidelines on the treatment of these diseases.

Assembly 8 – Thoracic surgery and Transplantation (Alberto Mendoza-Valderrey)

One of the highlights of the thoracic surgery and transplantation topics presented during the 2019 ERS International Congress was the symposium on “Lung transplantation (LT) in 2019: where are we?”. The importance of ethics in the field of lung transplantation was treated by Are Martin Holm (Oslo, Norway). Dirk Van Raemdonck (Leuven, Belgium) provided recommendations for maximising the organ donor pool, emphasising how the extracorporeal technology increases the number of viable donor lungs [47], besides improving the outcome after lung transplantation [48, 49]. In line with this, Geert Verleden (Leuven, Belgium) concluded that team expertise is an extremely important factor to improve long-term outcomes following lung transplantation [50].

In the poster discussion session “LT: from basic science to clinical outcomes”, PANDOLFI *et al.* [51] demonstrated that activated neutrophils induce the expression of the profibrotic microRNA miR-21 in bronchial epithelial cells, suggesting that this can be a possible therapeutic target in the context of bronchiolitis obliterans syndrome. Vall d’Hebron Lung Transplant Unit (Barcelona, Spain) shared their findings on a specific gene signature in peripheral blood from long-term survivors with

normal allograft function after LT [52, 53]. In addition, they also presented an integrated mRNA and microRNA transcriptomics profiling study that suggests that innate immune system may play a role in long-term survival after lung transplantation. Focusing on clinical studies, ULVESTAD *et al.* [54] showed how high-intensity training improves physical fitness and health outcomes after lung transplantation.

Other sessions in this assembly also focused on presenting general thoracic surgery aspects and the role of *ex vivo* lung perfusion, highlighting how this technique could improve donor organ quality.

Overall, these sessions highlighted the relationship between basic and clinical science in order to translate findings into clinical meaningful results with the goal of improving survival and quality of life of lung transplant recipients.

Assembly 12: interstitial lung diseases (Aurélien Justet)

During the 2019 ERS International Congress, several major therapeutic breakthroughs were presented. Two studies focussed on the efficacy of antifibrotic treatments or anti-interleukin (IL)-6 receptor antibody in progressive fibrosing ILD and in ILD related to systemic sclerosis (SSc). One study retrospectively assessed bronchoalveolar lavage (BAL) lymphocytosis in fibrotic hypersensitivity pneumonitis to predict corticosteroid treatment response.

The INBUILD trial, a double-blind, randomised, placebo-controlled study, assessed the efficacy and safety of nintedanib in patients with various non-idiopathic pulmonary fibrosis (IPF) chronic fibrosing ILDs with progressive phenotypes. Nintedanib significantly slowed the progression of ILD compared to placebo (difference in forced vital capacity (FVC) decline $107.0 \text{ mL}\cdot\text{year}^{-1}$, $p<0.001$) [55]. Safety profile in this population was similar with that observed in IPF population.

In ILD related to SSc, tocilizumab, an anti-IL-6 receptor antibody, showed clinically relevant lung function preservation but failed to improve the modified Ronan skin score endpoint. Conversely, the SENSICIS trial, a double-blind, randomised, placebo-controlled study, revealed that nintedanib significantly slowed the FVC decline of SSc patients treated with prednisone $<10 \text{ mg}\cdot\text{day}^{-1}$ and/or a stable therapy with mycophenolate mofetil or methotrexate [56].

Hypersensitivity pneumonitis is an ILD caused by sensitisation to an inhaled antigen. Distinguishing fibrotic hypersensitivity pneumonitis from nonfibrotic hypersensitivity pneumonitis is important, as the extent of histopathological fibrosis is associated with survival. One study assessed the impact of BAL lymphocytosis and honeycombing presence on corticosteroid treatment effect in 91 patients with fibrotic HP. It revealed that both low BAL lymphocyte count and honeycombing predicted

worse prognosis and the absence of a corticosteroid treatment effect [57].

Assembly 13: pulmonary vascular diseases (Junichi Omura)

In basic research, a study presented by Francois Potus provided further insight into the role of metabolic syndrome in the development of pulmonary hypertension (PH) due to left heart disease (LHD). He showed that precapillary PH due to diastolic dysfunction (induced by supracoronary aortic banding in rats) was exacerbated by a metabolic syndrome induced by high-fat diet and olanzapine. Mechanistically, he showed that pulmonary artery vascular remodelling resulted from an increase in circulating IL-6 due to an overproduction from both the macrophages and fat tissues. Hence, he showed that blocking IL-6 signalling improved PH-LHD [58].

A promising study by Takayuki Jujo demonstrated that gut microbiota was associated with the development of PH in SU5416/hypoxia (Su/Hx) rat model. Furthermore, PH in Su/Hx rats was attenuated by antibiotic treatment. There is increasing evidence demonstrating the pathogenic role of inflammation by microbiota in cardiovascular disease [59]. Taken together, these studies uncover novel mechanisms of the link between inflammation and the pathogenesis of PH.

In translational research, there was a pre-con debate session on current controversies in pulmonary artery denervation for PH. This session stimulated interest with hot topics, including the role of the sympathetic nervous system in PH and renal denervation for systemic hypertension.

Finally, the results from ASCO1 study (NCT01086540) were presented by ZAMANIAN [60]. This clinical trial was designed to assess the efficacy and safety of rituximab in SSc associated with PH. Although the first endpoint was negative in terms of improvement in 6-min walk distance (6MWD) at week 24, he showed the significant improvement of 6MWD at week 24 ($25.5\pm 8.8 \text{ m}$ rituximab, $0.4\pm 7.4 \text{ m}$ placebo; $p=0.03$) in a pre-specified secondary analysis that included only subjects who were followed until week 48. The clinical trial demonstrated that rituximab was a safe and potentially effective treatment for PH-SSc.

Assembly 14: clinical techniques, imaging and endoscopy (Karthi Srikanthan)

As in recent years, the 2019 ERS International Congress included a significant number of abstracts involving endoscopic techniques. Three

of the most interesting abstracts are discussed. Firstly, the AIRFLOW-2 trial (randomised, sham-controlled, double-blind trial of targeted lung denervation (TLD) in COPD) presented its 12-month outcomes. Similar to its 6-month data, there was a significant reduction in the number of patients who experienced severe COPD exacerbations in the TLD versus sham arm (12% versus 32%, $p=0.039$). This was also the case with respiratory-related serious adverse events (15% versus 37%, $p=0.042$). This well-designed trial continues to provide evidence that TLD is not only safe but also a signal that the denervation technique can be beneficial for patients with COPD. A larger pivotal trial is currently on-going in the USA and Europe [61]. Secondly, the TASMA trial (randomised, controlled trial of bronchial thermoplasty (BT) in severe asthma) measured airway smooth muscle (ASM) mass in endobronchial biopsies before and 6 months after BT treatment. Whilst BT has previously been shown to reduce ASM mass, this has never been studied using a control group. Using a crossover design, the TASMA trial demonstrated significant ASM mass reduction after BT compared with standard care

at 6 months (-4.44% versus 0.01% , $p=0.02$) [62]. Lastly, metered CryoSpray is a novel bronchoscopic treatment for chronic bronchitis. Using the RejuvenAir system (CSA Medical Inc., Lexington, MA, USA), liquid nitrogen is aerosolised and applied to the bronchial airways to ablate abnormal epithelium and promote regeneration of a healthy mucosal lining. The aim of the treatment is to improve quality of life by targeting mucous overproduction. In a multicentre, single-arm study, there was a clinically meaningful improvement in St George's Respiratory Questionnaire total score of -7.9 ± 16.8 (95% CI -14.2 to -1.6 , $p=0.008$) [63].

Concluding remarks

We hope to reach out to and inspire all clinicians and researchers to submit an abstract for the ERS International Congress 2020 (Vienna, Austria) as this gives them an opportunity to be elected as the 2020 Best Abstract awardee of their assembly. Abstract submission is open until 13 February 2020. Good luck!

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Conflict of interest

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